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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/767,758	01/29/2004	Paul M. Ridker	HA0801 NP	5405

23914 7590 01/17/2007

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EXAMINER	
KWON, BRIAN YONG S	
ART UNIT	PAPER NUMBER
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/767,758	RIDKER ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Acknowledgement is made of applicant's Response filed 10/31/06 in response to O.A. mailed 08/03/06.

2. By Amendment filed 10/31/06, claim 1 has been amended. Claims 1-8 are currently pending for prosecution on the merits of the instant application.

Summary of Action

3. The rejection of claims 1-6 under 35 U.S.C. 102(b) as being anticipated by Ridker (Vascular Medicine, 1998, 3: 67-73) is maintained for the reasons of record.

4. The rejection of claims 7-8 under 35 U.S.C. 103(a) as being unpatentable over Ridker (Vascular Medicine, 1998, 3: 67-73), and further in view of Milenson et al. (Blood, Vol. 79, No. 8, 1992: pp. 2034-2038) is maintained for the reasons of record.

5. Applicant's amendment requiring "which includes full-dose warfarin 2.0 to 3.0 INR" necessitates a new ground of rejection in this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-8 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Newly amended claim 1 recites the phrase "standard therapy which includes full-dose warfarin of 2.0 to 3.0 INR" in line 3.

Since the interpretation of the instant claims allow for the inclusion of other known therapy (other than "full-dose warfarin of 2.0 to 3.0 INR") by reciting "includes", the claims leave the reader in doubt as to the meaning of the invention to which they refer, thereby rendering the definition of the subject-matter of said claims unclear. Although the specification discloses that therapy for idiopathic venous thromboembolism (VTE) typically includes "a 5 to 10 day course of intravenous or subcutaneous heparin followed by a 3 to 12 month period of oral anticoagulation with full dose warfarin, adjusting the dosage to an international normalized ratio (INR) between 2.0 and 3.0", it is considered that the meaning of the claims should be clear from the wording of the claim alone.

The applicant could overcome this rejection by amending the phrase to "standard therapy involving 3 to 12 months of full-dose warfarin using a targeted International Normalized Ratio (INR) between 2.0 and 3.0 for venous thromboembolism".

Claim 1 recites the limitations "standard therapy which includes full-dose warfarin of 2.0 to 3.0 INR for venous thromboembolism" and "standard therapy for venous thromboembolism" in line 3 and line 5 respectively. It is not clear what "standard therapy for venous thromboembolism" in line 5 refers to. Does it refer to "standard therapy...for venous thromboembolism" in line 3? For proper antecedent basis, "standard therapy for venous thromboembolism" in line 5 should be corrected as "said standard therapy for venous thromboembolism".

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Ridker (Vascular Medicine, 1998, 3: 67-73). This rejection is analogous to the previous rejection mailed 08/03/06.

Ridker teaches the use of long-term (3-4 year regimen), low dose warfarin (INR 1.5-2.0) in patient with deep venous thrombosis and pulmonary embolism who undergone a 3-6 month period of full dose warfarin for preventing or reducing incidence of recurrent venous thromboembolism (abstract; page 71, column 1, lines 6-10 and 18-26), wherein the range of low-dose warfarin is as small as 1-2mg daily (page 70, column 1, line 14-19).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ridker (Vascular Medicine, 1998, 3: 67-73), and further in view of Milenson et al. (Blood, Vol. 79, No. 8, 1992: pp. 2034-2038). This rejection is analogous to the previous rejection mailed 08/03/06.

The teaching of Ridker has been discussed in above 35 USC 102(b) rejection.

Milenson is being supplied as a supplemental reference to demonstrate the routine knowledge in the art in determining "low dose of warfarin" to achiever the target INR range of 1.3 to 1.6. The reference teaches the use of mean daily dose 3.7 mg of warfarin in normal patient or mean 5.5mg of warfarin in patient who is on medications known to decrease the bioavailability of warfarin in achieving the targeted INR range of 1.3 to 1.6 (page 2035, column 2, lines 28-43).

The teaching of Rdiker differs from the claimed invention in the specific dosage of warfarin, "within the range from about 3 to about 6 mg daily" and "about 4 mg daily". '

However, those of ordinary skill in the art would have been readily determine effective dosages as determined by good medical practice and the clinical condition of the individual patient. Regardless of the manner of administration, the specific dose may be calculated according to body weight, body surface area or organ size. Further refinement of the calculations

necessary to determine the appropriate dosage for treatment involving each of the above mentioned formulations is routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation, especially in light of the dosage information herein. Appropriate dosages may be ascertained through use of established assays for determining dosages in conjunction with appropriate dose-response data. The final dosage regimen will be determined by the attending physician, considering the drug's specific activity, the responsiveness of the subject, the age, condition, body weight, diet, the severity of any infection, time of administration and other clinical factors. As evidenced by Milenson, those of ordinary skill in the art would be able to determine appropriate low dosage levels of warfarin which lies within the range of the claimed dosage range, "from about 3 to about 6mg daily" or "about 4mg daily" in achieving the targeted INR range of 1.5-2.0.

Response to Arguments

9. Applicant's arguments filed 10/31/06 have been fully considered but they are not persuasive.

Applicant's argument in the response takes the position that Ridker discloses a protocol for the PREVENT study and describes the design used in the study. The applicant asserts that there is no disclosure or suggestion in Ridker of whether use of long-term low-dose warfarin will be effective in the secondary prevention of venous thromboembolism.

This argument is not found persuasive. Anticipation under 35 USC 102 is an essentially irrebuttable question of fact if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. There is no efficacy standard requirement for the rejection under 35 USC 102. As discussed in the previous O.A. mailed

08/03/06 (page 3), Ridker teaches each and every elements as set forth in the instant claims: the use of long-term (3-4 year regimen), low dose warfarin (INR 1.5-2.0) in patient with deep venous thrombosis and pulmonary embolism who undergone a 3-6 month period of full dose warfarin for preventing or reducing incidence of recurrent venous thromboembolism (abstract; page 71, column 1, lines 6-10 and 18-26), wherein the range of low-dose warfarin is as small as 1-2mg daily (page 70, column 1, line 14-19). Thus, the examiner maintains that Ridker anticipates the claimed invention.

The court stated that anticipation "cannot be overcome by evidence of unexpected results or teachings away in the art. *In re Malagari, 499 F.2d 1289, 182 USPQ; In re Spada, 911 F.2d 705, 15 USPQ2d 1655 (Fed. Cir. 1990); In re Fracalossi, 681 F.2d 792, 215 USPQ 569 (CCPA 1982); In re Alternpohl, 500 F.2d 1151, 183 USPQ 38 (CCPA 1974); In re Wiggins, 488 F.2d 538, 179 USPQ 421 (CCPA 1973); In re Wilder, 429 F.2d 447, 166 USPQ 545 (CCPA 1970).* Indeed, a reference might reside in a nonanalogous art and yet constitute an anticipation of a claimed invention under 35 USC 102. *In re Self, 571 F.2d 134, 213 USPQ 1 (CCPA 1982).*

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the skilled artisan would have understood as taught by Millenson (who teaches the

use of mean daily dose 3.7 mg of warfarin in normal patient or mean 5.5mg of warfarin in patient who is on medications known to decrease the bioavailability of warfarin in achieving the targeted INR range of 1.3 to 1.6) that the Ridker's "low dose of warfarin (INR 1.5-2.0)" is within the prior art range. Thus, the cited references in combination make obvious the instant invention.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. No Claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Brian Kwon
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